chemotaxis is inhibited as a consequence of increased macrophage spreading. Macrophage spreading is known to be one step of a series which leads to complete macrophage activation [28]. What this theory suggests is that TFF initiates an early phase in the sequence of macrophage activation and thereby immobilizes them. This results paradoxically in facilitation of tumor development.

Various degrees of macrophage activation have been defined. Thiolglycollate-activated macrophages will spread rapidly but are not tumoricidal unless incubated with endotoxin [29]. However, macrophages stimulated with BCG, MAF, *Toxoplasma gondii*, or *Corynebacterium parvum* are cytotoxic to tumor cells including B16 [29–32]. Thiolglycollate-induced peritoneal macrophages enhance B16 tumor development when injected s.c. with an inoculum of B16 cells [32]. While the exact level to which TFF activates the macrophage is yet to be determined, there is a precedent for partial activation of the macrophages.

It is not proved that the TFF and the macrophage spreading activity are the same molecule. However, there is a strong correlation between macrophage spreading and tumor facilitation. Both activities are systemic, and both are effective in nude mice. Tumor facilitation, inhibition of macrophage accumulation, and macrophage spreading are all induced by the same dose of material. In addition, the activities are present in both B16 culture supernatant and B16 tumor homogenate. The dose response curves for both tumor facilitation in vivo, and macrophage spreading in vitro show a supraoptimal range, in which the effects of these activities are reversed. Supraoptimal concentrations of TFF are not toxic to macrophages in vitro as measured by phagocytosis of sheep erythrocytes. Finally, the injection of viable B16 cells was previously [1] found to facilitate the development of tumors at distant sites. Macrophage spreading was also induced under these conditions. Thus, both TFF and macrophage spreading activity are produced by B16 cells in vivo. Although it is not proved that TFF and macrophage spreading activity are the same molecule, the correlation between these activities is strong.

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